

5 What is claimed is:

1. A recombinant cell comprising:

(i) a receptor that, upon ligand stimulation, activates an endogenous signal transduction pathway; and

10 (ii) a heterologous DNA construct comprising a gene encoding a protein that activates the signal transduction pathway, which gene is operatively linked to a promoter that is responsive to activation of the signal transduction pathway; wherein stimulation of the receptor by a ligand leads to expression of the heterologous DNA construct encoding the protein that activates the signal transduction pathway such  
15 that signals generated by ligand binding to the receptor are amplified.

2. The cell of claim 1, which is a yeast cell.

3. The cell of claim 1, which is a mammalian cell.

20

4. The cell of claim 1, wherein the receptor is a G protein coupled receptor.

5. The cell of claim 4, wherein the G protein coupled receptor is a heterologous G protein coupled receptor.

25

6. The cell of claim 1, wherein the endogenous signal transduction pathway is a mitogen activated protein kinase (MAPK) pathway.

7. The cell of claim 2, wherein the endogenous signal transduction pathway is a yeast pheromone response pathway.

30

8. A recombinant yeast cell comprising :

(i) a heterologous G protein coupled receptor that, upon ligand stimulation, activates an endogenous yeast pheromone response pathway; and

35 (ii) a heterologous DNA construct comprising a gene encoding a protein that activates the yeast pheromone response pathway, which gene is operatively linked to a promoter that is responsive to activation of the yeast pheromone response pathway

wherein stimulation of the receptor by a ligand leads to expression of the heterologous  
40 DNA construct encoding the protein that activates the yeast pheromone response pathway such that signals generated by ligand binding to the receptor are amplified.

10

15

20

25

30

35

40

18. The yeast cell of claim 17, wherein the mutant Ste4 protein has a mutation selected from the group consisting of G124D; W136G; W136R; ΔL138; W136R,L138F; and W136G,S151C.

19. The yeast cell of claim 14, wherein the hypersensitive mutant form is a mutant Ste11 protein.

20. The yeast cell of claim 19, wherein the mutant Ste11 protein has a T596I mutation (allele Ste11-4) or a P278S mutation (allele Ste11-1).

- 5 21. The yeast cell of claim 14, wherein the hypersensitive mutant form is a mutant Fus3 protein.
22. The yeast cell of claim 21, wherein the mutant Fus3 protein has a I161L mutation.
- 10 23. The yeast cell of claim 8, wherein the promoter that is responsive to activation of the yeast pheromone response pathway is selected from the group consisting of: FUS1, AGA1, FAR1, and FUS2.
- 15 24. The yeast cell of claim 23, wherein the promoter is a FUS1 promoter.
25. The yeast cell of claim 8, wherein an endogenous yeast gene encoding a protein that negatively regulates the yeast pheromone system pathway is mutated to render the protein nonfunctional.
- 20 26. The yeast cell of claim 25, wherein the endogenous gene that is mutated encodes a phosphatase that negatively regulates the yeast pheromone system pathway.
- 25 27. The yeast cell of claim 26, wherein the endogenous gene encoding the phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.
28. The yeast cell of claim 8, which further comprises a reporter gene construct that produces a detectable signal upon activation of the yeast pheromone response pathway.
- 30 29. The yeast cell of claim 8, wherein the heterologous DNA construct is carried by a high copy number plasmid.
30. The yeast cell of claim 8, wherein the heterologous DNA construct is carried by a low copy number plasmid.
- 35 31. The yeast cell of claim 8, which is a *Saccharomyces cerevisiae* cell.
32. A recombinant yeast cell comprising :
- 40 (i) a heterologous G protein coupled receptor that, upon ligand stimulation, activates an endogenous yeast pheromone response pathway; and
- (ii) a heterologous DNA construct comprising a STE5 or STE4 gene encoding a Ste5 or Ste4 protein, respectively, that activates the yeast pheromone response

5 pathway, which gene is operatively linked to a FUS1 promoter that is  
responsive to activation of the yeast pheromone response pathway  
wherein stimulation of the receptor by a ligand leads to expression of the heterologous  
DNA construct encoding the Ste5 or Ste4 protein that activates the yeast pheromone  
response pathway such that signals generated by ligand binding to the receptor are  
10 amplified.

33. The yeast cell of claim 32, wherein the gene encodes a hypersensitive mutant  
form of the Ste5 or Ste4 protein that activates the yeast pheromone response pathway.

15 34. The yeast cell of claim 32, wherein an endogenous yeast gene encoding a protein  
that negatively regulates the yeast pheromone system pathway is mutated to render the  
protein nonfunctional.

35. The yeast cell of claim 34, wherein the endogenous gene that is mutated encodes  
20 a phosphatase that negatively regulates the yeast pheromone system pathway.

36. The yeast cell of claim 35, wherein the endogenous gene encoding the  
phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.

25 37. The yeast cell of claim 32, which further comprises a reporter gene construct that  
produces a detectable signal upon activation of the yeast pheromone response pathway.

38. The yeast cell of claim 32, wherein the heterologous DNA construct is carried by  
a high copy number plasmid.

30 39. The yeast cell of claim 32, wherein the heterologous DNA construct is carried by  
a low copy number plasmid.

40. The yeast cell of claim 32, which is a *Saccharomyces cerevisiae* cell.

35 41. A recombinant yeast cell comprising:  
a heterologous G protein coupled receptor that, upon ligand stimulation,  
activates an endogenous yeast pheromone response pathway,  
wherein an endogenous yeast gene encoding a protein that negatively regulates the yeast  
40 pheromone system pathway is mutated to render the protein nonfunctional such that  
signals generated by ligand binding to the receptor are amplified.

42. The yeast cell of claim 41, wherein the endogenous gene that is mutated encodes a phosphatase that negatively regulates the yeast pheromone system pathway.

43. The yeast cell of claim 42, wherein the endogenous gene encoding the phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.

10

44. A recombinant yeast cell comprising :  
a heterologous G protein coupled receptor that, upon ligand stimulation,  
activates an endogenous yeast pheromone response pathway,  
wherein an endogenous FUS3 gene is mutated to encode a supersensitive form of Fus3  
protein such that signals generated by ligand binding to the receptor are amplified.

45. The yeast cell of claim 44, wherein the supersensitive form of Fus3 protein has a I161L mutation.

20

46. An assay to identify compounds that modulate the activity of a receptor, comprising:

(i) providing a recombinant cell as claimed in claim 1, 8, 32, 41 or 44, wherein a detectable signal is produced in the cell upon stimulation of the receptor;

(ii) contacting the cell with a test compound; and

25

(iii) identifying a compound which induces a change in the detectable signal in the cell, such a change indicating that the compound modulates the activity of the receptor.

47. The assay of claim 46, wherein the cell comprises a reporter gene construct that produces a detectable signal upon receptor stimulation.

30

~~add B<sub>1</sub>~~